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 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  JUL 02   LMEDLINE coverage updated
 NEWS  3  JUL 02   SCISEARCH enhanced with complete author names
 NEWS  4  JUL 02   CHEMCATS accession numbers revised
 NEWS  5  JUL 02   CA/CAplus enhanced with utility model patents from China
 NEWS  6  JUL 16   CAplus enhanced with French and German abstracts
 NEWS  7  JUL 18   CA/CAplus patent coverage enhanced
 NEWS  8  JUL 26   USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS  9  JUL 30   USGENE now available on STN
 NEWS 10  AUG 06   CAS REGISTRY enhanced with new experimental property tags
 NEWS 11  AUG 06   BEILSTEIN updated with new compounds
 NEWS 12  AUG 06   FSTA enhanced with new thesaurus edition
 NEWS 13  AUG 13   CA/CAplus enhanced with additional kind codes for granted
                   patents
 NEWS 14  AUG 20   CA/CAplus enhanced with CAS indexing in pre-1907 records
 NEWS 15  AUG 27   Full-text patent databases enhanced with predefined
                   patent family display formats from INPADOCDB
 NEWS 16  AUG 27   USPATOLD now available on STN
 NEWS 17  AUG 28   CAS REGISTRY enhanced with additional experimental
                   spectral property data
 NEWS 18  SEP 07   STN AnaVist, Version 2.0, now available with Derwent
                   World Patents Index
 NEWS 19  SEP 13   FORIS renamed to SOFIS
 NEWS 20  SEP 13   INPADOCDB enhanced with monthly SDI frequency
 NEWS 21  SEP 17   CA/CAplus enhanced with printed CA page images from
                   1967-1998
 NEWS 22  SEP 17   CAplus coverage extended to include traditional medicine
                   patents
 NEWS 23  SEP 24   EMBASE, EMBAL, and LEMBASE reloaded with enhancements

 NEWS EXPRESS  19 SEPTEMBER 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE 'HOME' ENTERED AT 15:59:07 ON 25 SEP 2007

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE COVERS 1907 - 25 Sep 2007 VOL 147 ISS 14
FILE LAST UPDATED: 24 Sep 2007 (20070924/ED)

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http://www.cas.org/infopolicy.html

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=> s 103146-25-4/rn
            25 103146-25-4
             0 103146-25-4D
L1           25 103146-25-4/RN
                (103146-25-4 (NOTL) 103146-25-4D )

=> s l1 and (?purif? or ?crystall? or ?resolut?)
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        552440 ?CRYST
        613879 ?CRYSTALL?
        552440 ?CRYST
        361796 CRYST
          1801 CRYSTS
        363064 CRYST
                (CRYST OR CRYSTS)
        140380 ?CRYSTD
         92700 CRYSTD
         26420 ?CRYSTG
         20119 CRYSTG
        314891 ?CRYSTN
        244026 CRYSTN
          2426 CRYSTNS
        245345 CRYSTN
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                (CRYSTN OR CRYSTNS)
       1221909 ?CRYSTALL?
                (?CRYSTALL? OR ?CRYST OR CRYST OR ?CRYSTD OR CRYSTD OR ?CRYSTG
                 OR CRYSTG OR ?CRYSTN OR CRYSTN)
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        103777 ?RESOLUT?
        328729 ?RESOLN
        328169 RESOLN
          7799 RESOLNS
        332327 RESOLN
                (RESOLN OR RESOLNS)
        374290 ?RESOLUT?
                (?RESOLUT? OR ?RESOLN OR RESOLN)
L2          19 L1 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)

=> d scan

L2    19 ANSWERS   CAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  C07D307-00
CC    27-7 (Heterocyclic Compounds (One Hetero Atom))
      Section cross-reference(s): 1
TI    Process for purification of citalopram via washing with
      polybasic acid solutions
ST    citalopram purifn polybasic acid wash;
      dimethylaminopropylfluorophenyldihydroisobenzofurancarbonitrile
      purifn polybasic acid wash
IT    Acids, reactions
      RL: RGT (Reagent); RACT (Reactant or reagent)
         (polybasic; process for purification of citalopram via washing
         with polybasic acid solns.)
IT    5-HT reuptake inhibitors
         (process for purification of citalopram)
IT    59729-33-8P, Citalopram
      RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN
      (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
      PREP (Preparation); USES (Uses)
         (process for purification of citalopram)
IT    75-09-2, Methylene chloride, uses   108-88-3, Toluene, uses   110-54-3,
      Hexane, uses   141-78-6, Ethyl acetate, uses
      RL: NUU (Other use, unclassified); USES (Uses)
         (process for purification of citalopram via washing with polybasic
         acid solns.)
IT    59729-32-7P, Citalopram hydrobromide
      RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN
      (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
      PREP (Preparation); USES (Uses)
         (process for purification of citalopram via washing with polybasic
         acid solns.)
IT    60-00-4, Edetic acid, reactions   77-92-9, Citric acid, reactions
      87-69-4, Tartaric acid, reactions   110-17-8, Fumaric acid, reactions
      124-63-0, Methanesulfonyl chloride   139-33-3   144-62-7, Oxalic acid,
      reactions   64169-39-7 103146-25-4   488787-59-3
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (process for purification of citalopram via washing with polybasic
         acid solns.)
IT    1310-58-3, Potassium hydroxide, reactions   1310-73-2, Sodium hydroxide,
      reactions
      RL: RGT (Reagent); RACT (Reactant or reagent)
         (process for purification of citalopram via washing with polybasic
         acid solns.)
```

```
IT   128196-01-0P, Escitalopram
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (process for purification of citalopram via washing with polybasic
        acid solns.)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s 59729-33-8/rn
          2067 59729-33-8
            17 59729-33-8D
L3          2061 59729-33-8/RN
                 (59729-33-8 (NOTL) 59729-33-8D )

=> s l3 and (?purif? or ?crystall? or ?resolut?)
         855980 ?PURIF?
         552440 ?CRYST
         613879 ?CRYSTALL?
         552440 ?CRYST
         361796 CRYST
           1801 CRYSTS
         363064 CRYST
                  (CRYST OR CRYSTS)
         140380 ?CRYSTD
          92700 CRYSTD
          26420 ?CRYSTG
          20119 CRYSTG
         314891 ?CRYSTN
         244026 CRYSTN
           2426 CRYSTNS
         245345 CRYSTN
                  (CRYSTN OR CRYSTNS)
        1221909 ?CRYSTALL?
                  (?CRYSTALL? OR ?CRYST OR CRYST OR ?CRYSTD OR CRYSTD OR ?CRYSTG
                   OR CRYSTG OR ?CRYSTN OR CRYSTN)
         328729 ?RESOLN
         103777 ?RESOLUT?
         328729 ?RESOLN
         328169 RESOLN
           7799 RESOLNS
         332327 RESOLN
                  (RESOLN OR RESOLNS)
         374290 ?RESOLUT?
                  (?RESOLUT? OR ?RESOLN OR RESOLN)
L4          112 L3 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)

=> s l3 not l4
L5          1949 L3 NOT L4

=> d his

     (FILE 'HOME' ENTERED AT 15:59:07 ON 25 SEP 2007)

     FILE 'CAPLUS' ENTERED AT 15:59:19 ON 25 SEP 2007
L1            25 S 103146-25-4/RN
L2            19 S L1 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)
L3          2061 S 59729-33-8/RN
L4           112 S L3 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)
L5          1949 S L3 NOT L4

=> s l4 not l3
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L6            0 L4 NOT L3

=> d scan l2 1-19


=> d his

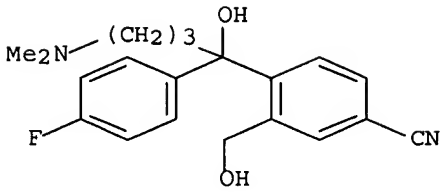
     (FILE 'HOME' ENTERED AT 15:59:07 ON 25 SEP 2007)

     FILE 'CAPLUS' ENTERED AT 15:59:19 ON 25 SEP 2007
L1           25 S 103146-25-4/RN
L2           19 S L1 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)
L3         2061 S 59729-33-8/RN
L4          112 S L3 AND (?PURIF? OR ?CRYSTALL? OR ?RESOLUT?)
L5         1949 S L3 NOT L4
L6            0 S L4 NOT L3

=> d ibib abs hitstr l2 1-19

L2   ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:797954  CAPLUS  Full-text
DOCUMENT NUMBER:          147:277422
TITLE:                    Method for producing high-purity citalopram via
                          Grignard and cyclization reactions
INVENTOR(S):              Szabadkai, Istvan
PATENT ASSIGNEE(S):       Hung.
SOURCE:                   Hung. Pat. Appl., 22pp.
                          CODEN: HUXXCV
DOCUMENT TYPE:            Patent
LANGUAGE:                 Hungarian
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     HU 200301605          A2    20051128    HU 2003-1605             20030605
     HU 225533             B1    20070228
PRIORITY APPLN. INFO.:                       HU 2003-1605             20030605
AB   Process to prepare a high-purity citalopram base via Grignard reaction of 5-
     cyano-phthalide with 4-fluorophenyl-magnesium bromide, then with
     dimethylamino-magnesium chloride at 25-45°C, with the controlled addition of
     the reagents and cyclization reaction using 60% phosphoric acid. The oily or
     solid raw citalopram base is trans-crystallized twice out of aqueous alc.
     during treatment with activated carbon.
IT   103146-25-4P
     RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
     preparation); PREP (Preparation); RACT (Reactant or reagent)
        (method for producing highpurity citalopram via Grignard and
        cyclization reactions)
RN   103146-25-4  CAPLUS
CN   Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-
     (hydroxymethyl)-  (CA INDEX NAME)
```



L2 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:115433 CAPLUS Full-text
DOCUMENT NUMBER: 146:206191
TITLE: An improved process for preparation of escitalopram
INVENTOR(S): Kaushik, Vipin Kumar; Khan, Mohammed Umar; Meenakshisunderam, Sivakumaran
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: PCT Int. Appl., 18pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

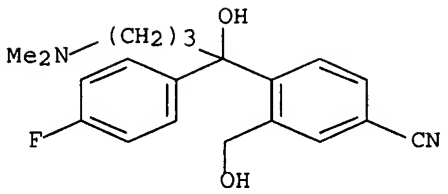
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007012954	A1	20070201	WO 2006-IB2050	20060720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005CH01014	A	20070720	IN 2005-CH1014	20050727

PRIORITY APPLN. INFO.: IN 2005-CH1014 A 20050727
OTHER SOURCE(S): CASREACT 146:206191

AB The present invention relates to an improved process for the preparation of escitalopram, which comprises purification and optical resoln . of 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile to obtain the S-enantiomer, followed by cyclization to give escitalopram with 99.12% purity. The process has the advantages of high yield and high purity.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of escitalopram)

RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1356784 CAPLUS Full-text
DOCUMENT NUMBER: 146:80528
TITLE: Chemoenzymatic process for the synthesis of escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul; Bertoni, Chiara
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

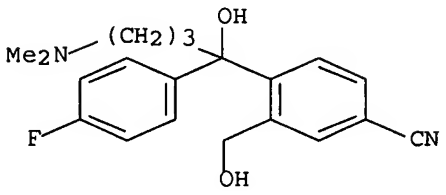
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006136521	A1	20061228	WO 2006-EP63193	20060614
WO 2006136521	A8	20070308		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1736550	A1	20061227	EP 2005-425452	20050622
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

PRIORITY APPLN. INFO.: EP 2005-425452 A 20050622
US 2005-697398P P 20050706
OTHER SOURCE(S): CASREACT 146:80528; MARPAT 146:80528

AB A process is described for the preparation of escitalopram and the pharmaceutically acceptable salts thereof starting from 5-cyanophthalide by a process which provides an enantioselective enzymic deacylation reaction of a complex of the formula (IV) where R represents a C1-C4 alkyl residue or an aryl residue under the action of an esterase from Aspergillus niger.

IT 103146-25-4P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(chemoenzymic process for synthesis of escitalopram)
RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1298672 CAPLUS Full-text

DOCUMENT NUMBER: 146:302669

TITLE: Enantiospecific assay of citadiol, a key intermediate of escitalopram by liquid chromatography on Chiralpak AD-H column connected with UV and polarimetric detectors in series

AUTHOR(S): Rao, R. Nageswara; Raju, A. Narasa

CORPORATE SOURCE: HPLC/UV Group, Division of Analytical Chemistry, Discovery Laboratory, Indian Institute of Chemical Technology, Hyderabad, 500007, India

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2007), 43(1), 311-314
CODEN: JPBADA; ISSN: 0731-7085

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

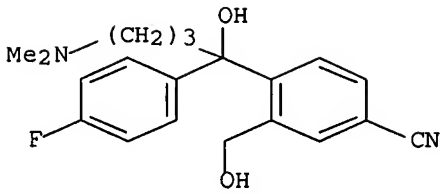
LANGUAGE: English

AB A simple, rapid, selective and reproducible LC method for separation and quant. determination of citadiol (CTD), a key intermediate of escitalopram has been developed. An optimum resolution >3.0 was achieved on Chiralpak AD-H (250 mm + 4.6 mm); 5 μm column connected with UV and polarimetric detectors in series. The effects of organic modifiers, viz., methanol, ethanol, n-propanol and 2-propanol on enantioselectivity were evaluated. The limits of detection and quantification were 0.02 μg/mL, 0.03 μg/mL and 0.07 μg/mL, 0.10 μg/mL for R-CTD and S-CTD enantiomers, resp. The linearity of the method was studied in the range of 0.07-300 μg/mL and 0.1-300 μg/mL for R-CTD and S-CTD, resp. and the r 2 was ≥0.9999. The inter- and intra-day assay precision was less than 0.74% (%R.S.D.) and the recoveries were in the range 99.68-100.72% with %R.S.D. <0.49%.

IT 103146-25-4, Citadiol
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(enantiospecific assay of citadiol, a key intermediate of escitalopram, by liquid chromatog.)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



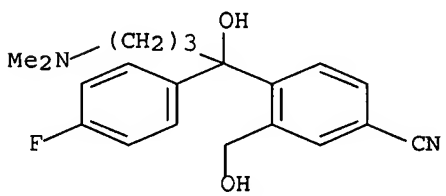
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:883762 CAPLUS Full-text
DOCUMENT NUMBER: 147:257599
TITLE: Synthesis of escitalopram oxalate
AUTHOR(S): Yao, Zhong-ke; Kan, Li-juan
CORPORATE SOURCE: Department of Chemistry, Capital Normal University, Beijing, 100037, Peop. Rep. China
SOURCE: Zhongguo Xinyao Zazhi (2006), 15(2), 117-120
CODEN: ZXZHA6; ISSN: 1003-3734
PUBLISHER: Zhongguo Xinyao Zazhi Youxian Gongsi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The synthesis of escitalopram oxalate [i.e., (1S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile ethanedioate] is reported. Starting from 5-cyanophthalide, escitalopram oxalate was prepared via several steps including nucleophilic addition, hydrolysis, chemical separation, cyclization and salt formation. A total yield of escitalopram oxalate was 13.6%. This easily manipulated synthetic process is worthy of further pilot manufacturing studies.

IT 103146-25-4P, 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of escitalopram oxalate via synthetic sequence involving nucleophilic addition, hydrolysis, resolution, cyclization and salt formation)

RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

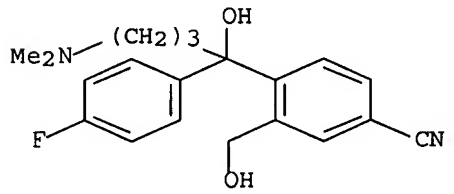


L2 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:827174 CAPLUS Full-text
DOCUMENT NUMBER: 146:500809
TITLE: An improved resolution process for the preparation of antidepressant drug: escitalopram

AUTHOR(S): Mital, Alka; Kumar, Rakesh; Ramachandran, Uma
CORPORATE SOURCE: Department of Pharmaceutical Technology, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, 160062, India
SOURCE: Organic Preparations and Procedures International (2006), 38(4), 423-426
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:500809

AB Efficient resolution process for the intermediate racemic diol 4-(4-dimethylamino)-1-(4'-fluorophenyl)-1-(hydroxybutyl)-3-(hydroxymethyl)benzonitrile, wherein the S-diol is obtained in pure form, which is basified and then cyclized to give S-citalopram of >99 % enantiomeric purity. The method provides an easy way to improve the enantiomeric purity of S-citalopram that is obtained by diastereomeric salt crystallization method as compared to the other processes. The novelty of this process is that the enriched diastereomeric salt is crystallized twice using a medium polar solvent, before it is released as a free base. This avoids the cumbersome two stage purification process of the other reported processes.

IT 103146-25-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved resolution process for preparation of escitalopram as antidepressant drug)
RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:342904 CAPLUS Full-text
DOCUMENT NUMBER: 144:390731
TITLE: Intramolecular cyclocondensation process for the preparation of citalopram and escitalopram
INVENTOR(S): Cotticelli, Giovanni; Salvetti, Raul
PATENT ASSIGNEE(S): Adorkem Technology SpA, Italy
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006037714 A2 20060413 WO 2005-EP54566 20050914
WO 2006037714 A3 20060727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
CA 2581195 A1 20060413 CA 2005-2581195 20050914
EP 1794140 A2 20070613 EP 2005-789627 20050914
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU
IN 2007DN02442 A 20070504 IN 2007-DN2442 20070330
PRIORITY APPLN. INFO.: IT 2004-MI1872 A 20041001
WO 2005-EP54566 W 20050914

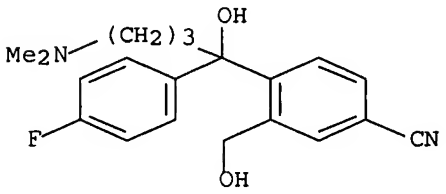
OTHER SOURCE(S): CASREACT 144:390731; MARPAT 144:390731

AB A process is described for the preparation of citalopram and of the enantiomer escitalopram which comprises the intramol. cyclocondensation of the corresponding glycol or its chiral enantiomer using the Mitsunobu reaction with an azodicarboxylate diester, a phosphine, and a strong base.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(intramol. cyclocondensation process for the preparation of citalopram and escitalopram)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

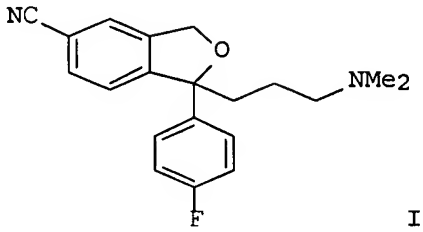


L2 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:332704 CAPLUS Full-text
DOCUMENT NUMBER: 144:331251
TITLE: Chemoenzymatic synthesis of (+)-citalopram and (-)-citalopram by kinetic resolution of diol and diol monoester intermediates using esterification or hydrolysis in the presence of Candida antarctica lipase B
INVENTOR(S): Bayod Jasanada, Miguel; Llorente Garcia, Isidro; Gotor Santamaria, Vicente; Brieva Collado, M. Rosario; Fernandez Solares, Laura; Quiros Alvarez, Margarita
PATENT ASSIGNEE(S): Astur Pharma, S.A., Spain; Universidad de Oviedo
SOURCE: Span., 14 pp.

CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2228274	A1	20050401	ES 2003-2215	20030924
ES 2228274	B1	20060601		

PRIORITY APPLN. INFO.: ES 2003-2215 20030924
OTHER SOURCE(S): CASREACT 144:331251; MARPAT 144:331251
GI



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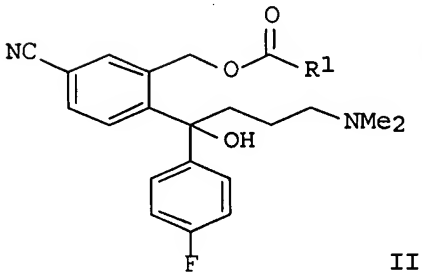
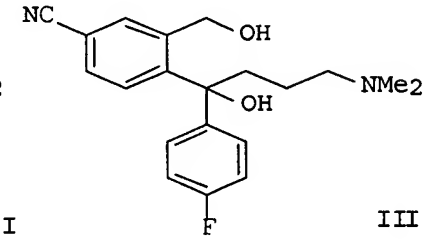


II



III

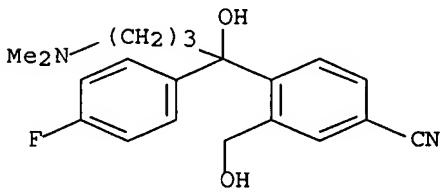
AB New processes and intermediates for the preparation of (S)-(+)- and (R)-(-)-citalopram, i.e., (+)- and (-)-I, are disclosed. The claimed intermediates include the optically enriched diol monoesters (+)- and (-)-II, as well as the diols (+)- and (-)-III [wherein: R1 = alkyl or aryl]. The claimed processes include two types of kinetic resoln .: (1) enzymic acylation of racemic diol (±)-III with an acylating agent R1CO2R2 [R1 = alkyl or aryl; R2 = alkyl, alkenyl or aryl], to give (R)-(+)-II and (S)-(-)-III; and (2) enzymic hydrolysis of the racemic ester (±)-II, to give (S)-(-)-II and (R)-(+)-III. The enzyme catalyst is a hydrolase, especially a lipase, and most particularly, fraction B of the lipase of Candida antarctica (IV). Five examples are given; these cover both of the aforementioned processes, as well as hydrolysis of a monoester resolution product, and the conversion of both III enantiomers to the corresponding I enantiomers. For instance, reaction of (±)-III with vinyl acetate in MeCN in the presence of immobilized IV at 30° for 20 h gave (S)-(-)-III in 47% yield and >99% enantiomeric excess, along with some (R)-(+)-II (R1 = Me) with >90% ee. Cyclization of (S)-(-)-III by slow treatment with mesyl chloride in CH2Cl2 at 0°, followed by stirring for 1 h at 15°, gave (S)-(+)-I in 90% yield and >99% ee.

IT 103146-25-4, 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)

(kinetic resolution; chemoenzymic preparation of (+)- and (-)-citalopram by kinetic resolution of diol and diol monoester intermediates using transesterification or hydrolysis in presence of Candida antarctica lipase B)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



L2 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:220981 CAPLUS Full-text

DOCUMENT NUMBER: 145:103520

TITLE: Preparation and purification of Citalopram salts

INVENTOR(S): Liu, Zhiping; Huang, Weipeng; Yuan, Aiguo; Xiao, Keqiang; Li, Youcheng; Zhuang, Jingfa

PATENT ASSIGNEE(S): Guangdong Xilong Chemical Co., Ltd., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1740167	A	20060301	CN 2005-10035699	20050712

PRIORITY APPLN. INFO.: CN 2005-10035699 20050712

OTHER SOURCE(S): CASREACT 145:103520

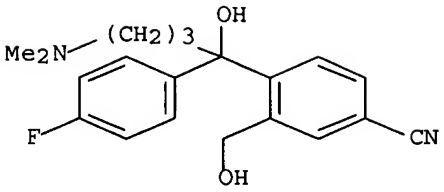
AB The invention provides a method for the preparation and purification of Citalopram salts, which comprises mixing an acid and Citalopram diol compound at molar ratio of (1-10):1 in toluene at 50-100° under stirring, and recrystg. in water and the diluted acid to obtain corresponding Citalopram salts with a purity above 99.5%; wherein the acid can be hydrobromic acid, hydrochloric acid, hydroiodic acid, hydrofluoric acid, p-toluenesulfonic acid, methylsulfonic acid, oxalic acid, formic acid, acetic acid, hydroxyacetic acid, tartaric acid, citric acid, malic acid, malonic acid, succinic acid, glutaric acid or adipic acid.

IT 103146-25-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of Citalopram salts)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



L2 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1075785 CAPLUS Full-text
DOCUMENT NUMBER: 143:347046
TITLE: Preparation of crystalline citalopram diol intermediate
INVENTOR(S): Mei, Runan; Guo, Dianwu; Wang, Shulong
PATENT ASSIGNEE(S): Hangzhou Minsheng Pharmaceutical Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092875	A1	20051006	WO 2004-CN1418	20041206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1629153	A	20050622	CN 2004-10044335	20040526
EP 1700851	A1	20060913	EP 2004-802432	20041206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 2007117992	A1	20070524	US 2006-583360	20060619
PRIORITY APPLN. INFO.:			CN 2003-10123623 A	20031219
			CN 2004-10044335 A	20040526
			WO 2004-CN1418 W	20041206

OTHER SOURCE(S): MARPAT 143:347046

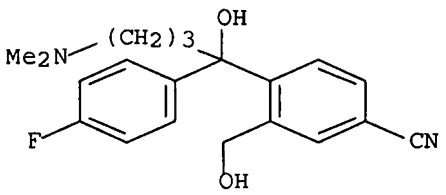
AB The invention relates to the diol intermediate of citalopram useful for treatment of depression, that is to say, the crystal of free base of 3-hydroxymethyl-4-[1-(4-fluorophenyl)-1-hydrorybutyl-4-(dimethylamino)]butylbenzonitrile, and the method of crystallization thereof. The invention has disclosed the method to prepare the pure citalopram, its purified salts, the optical resolution method of citalopram diol intermediate, the method to prepare S-citalopram and its purified salts by crystals mentioned above. The invention has also disclosed citalopram and its purified salts, (S)-citalopram and its purified salts, as well as pharmaceutical formulation thereof obtained. Using methods of the invention, the quality and

yield of the product can be signally improved, and production cost of the medicinal material can be decreased.

IT 103146-25-4P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation of citalopram diol intermediate)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:902848 CAPLUS Full-text
DOCUMENT NUMBER: 143:248161
TITLE: Method for the separation of intermediates which may be used for the preparation of escitalopram
INVENTOR(S): Lyngso, Lars Ole
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077891	A1	20050825	WO 2005-DK75	20050202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005212455	A1	20050825	AU 2005-212455	20050202
CA 2555980	A1	20050825	CA 2005-2555980	20050202
EP 1716108	A1	20061102	EP 2005-700625	20050202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1918112	A	20070221	CN 2005-80004594	20050202
BR 2005007580	A	20070731	BR 2005-7580	20050202

JP 2007524678	T	20070830	JP 2006-552461		20050202
MX 2006PA08977	A	20061020	MX 2006-PA8977		20060808
IN 2006CN02945	A	20070608	IN 2006-CN2945		20060810
NO 2006004086	A	20060912	NO 2006-4086		20060912
US 2007190624	A1	20070816	US 2006-597836		20061108
PRIORITY APPLN. INFO.:			DK 2004-217	A	20040212
			US 2004-544970P	P	20040212
			WO 2005-DK75	W	20050202

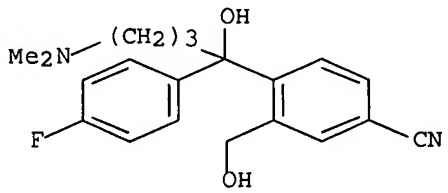
OTHER SOURCE(S): CASREACT 143:248161; MARPAT 143:248161
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I [R1 = H, or group II; R2 = CN, or a group which may be converted to CN; R3 = halo; X = double or single bond; Y = bond, O, S, or NH; W = O, or S; R4 = alkyl, alkenyl, alkynyl, aryl, hetroaryl, all of which may be optionally substituted with alkoxy, alkythio, halo, OH, NH, NO2, CN, alkylamino, aryl, aryloxy, arylthio, and heteroaryl], or a salt from a mixture of I [R1 = group II] and I [R1 = H], which was reacting with cyclic anhydride or imide to form a mixture of I [R1 = group II] and an esters III (R5 = substituted heteroaryl carboxylic acid), were prepared by enzymic acylation or deacylation, separated, isolated and purified and used for manufacturing of escitalopram and derivs. Compds. I [R1 = group II] were separated from esters III by precipitation of III from the mixture, or by partitioning between an organic solvent and aqueous solvent, by adsorbing I [R1 = group II] on a basic resin. Thus, addition of succinic anhydride to a mixture of butyric acid 5-cyano-2-[4-dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-benzyl ester and prepared by enzymic resolution 4-[(S)-4-dimethylamino-1-(4'- fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile, gave after precipitation and washing 2,02 g of escitalopram [(S)-1-(3-dimethylamino-propyl)-1- (4-fluoro-phenyl)-1,3-dihydro-isobenzofuran-5-carbonitrile] hydrogen oxalate (ee = 95%).

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation by enzymic acylation or deacylation, separation, isolation and purification by precipitation, partitioning, or adsorption, of benzonitriles
used as intermediates for synthesis of escitalopram and derivs.)

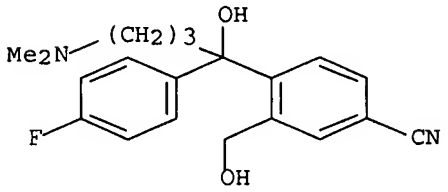
RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:687869 CAPLUS Full-text

DOCUMENT NUMBER: 144:78306
TITLE: 4-[4-Dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile
AUTHOR(S): Gu, Jian Ming; Wang, Yun Wu; Hu, Xiu Rong
CORPORATE SOURCE: Center of Analysis and Measurement, Zhejiang University, Zhejiang, 310028, Peop. Rep. China
SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2005), E61(8), o2691-o2693
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/issues/2005/08/00/ob6553/index.html
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the structure of the title compound, C20H23FN2O2, there are two independent mols. showing different conformations. The mols. form centrosym. dimers via O-H···N or O- H···O H bonds. Crystallog. data are given.
IT 103146-25-4P, 4-[4-Dimethylamino-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

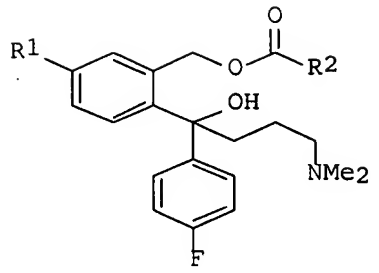


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:519249 CAPLUS Full-text
DOCUMENT NUMBER: 143:59681
TITLE: Process for the preparation of citalopram enantiomer
INVENTOR(S): Li, Lan; Li, Qian
PATENT ASSIGNEE(S): Dezhong Wanquan Pharmaceutical Technology Developing Co., Ltd., Beijing, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1510024	A	20040707	CN 2002-158181	20021224

PRIORITY APPLN. INFO.: CN 2002-158181 20021224
OTHER SOURCE(S): CASREACT 143:59681; MARPAT 143:59681
GI



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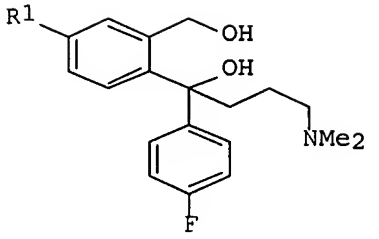


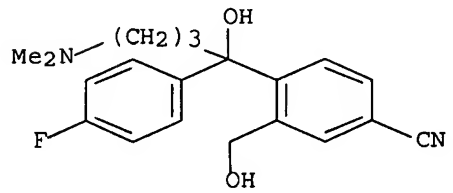
II

AB A process for the preparation of title compound, a drug as antidepressant, and the preparation of its intermediate I [R1 = CN, halo, alkoxy, alkylaminocarbonyl; R2 = amino containing group, amino containing aryl or cyclic ring] comprising reacting a compound of formula II with a compound of formula XCOR2 (R1, R2 are defined as above) is disclosed. For example, reaction of II (R1 = CN) with 2-chloronicotinic acid gave I (R1 = CN, R2 = 2-chloropyridin-3-yl) in 80% yield. Optical resolution of I by salification of I with di-p-toluoyl-L-tartaric acid , followed by recrystn. and hydrolysis, provided (S)-II. Cyclization of (S)-II gave optical active (S)-citalopram.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of citalopram enantiomer and its intermediate)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



L2 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:120910 CAPLUS Full-text

DOCUMENT NUMBER: 142:197860

TITLE: Process for purification of citalopram via washing with polybasic acid solutions

INVENTOR(S): Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan

PATENT ASSIGNEE(S): Meditab Specialities Pvt. Ltd., India; Wain, Christopher Paul

SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

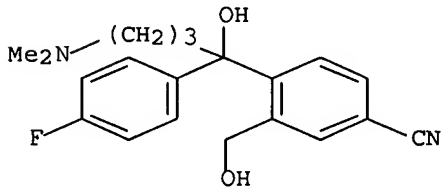
WO 2005012278 A2 20050210 WO 2004-GB3209 20040723
WO 2005012278 A3 20050616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
GB 2418916 A 20060412 GB 2006-1023 20040723
DE 112004001368 T5 20060629 DE 2004-112004001368 20040723
IN 2006MN00092 A 20061006 IN 2006-MN92 20060124
US 2006189816 A1 20060824 US 2006-565736 20060419
PRIORITY APPLN. INFO.: GB 2003-17475 A 20030725
WO 2004-GB3209 W 20040723

OTHER SOURCE(S): CASREACT 142:197860

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1- (4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc layer was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for purification of citalopram via washing with polybasic acid solns.)

RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



L2 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:878385 CAPLUS Full-text
DOCUMENT NUMBER: 141:366120
TITLE: Process for the preparation of 5-bromophthalide via reduction of 4-bromophthalic anhydride.
INVENTOR(S): Oren, Jacob
PATENT ASSIGNEE(S): Bromine Compounds Ltd., Israel
SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089924	A1	20041021	WO 2003-IB1450	20030411

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

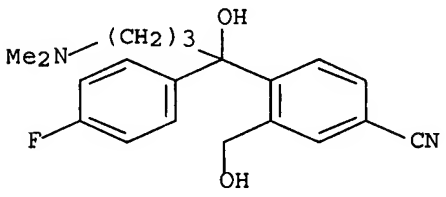
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003214582	A1	20041101	AU 2003-214582	20030411

PRIORITY APPLN. INFO.: WO 2003-IB1450 A 20030411
OTHER SOURCE(S): CASREACT 141:366120

AB A process for preparation of 5-bromophthalide comprises reducing 4-bromophthalic anhydride in an organic solvent to obtain a mixture of 5-bromophthalide and 6-bromophthalide, acidifying the reaction mixture, separation of aqueous and organic phases, and selectively crystallizing 5-bromophthalide from the organic phase. Thus, 4-bromophthalic anhydride in THF was added to a slurry of NaBH4 in THF at 5° over 2.5 h followed by stirring for 1 h at 25°. H2O and aqueous HCl were added to pH 1-2 followed by heating to 58°, phase separation, partial distillation of solvent, and crystallization of crude 5-bromophthalide by adding H2O and cooling to 30°. The resulting product was recrystd. from aqueous THF to give 98% pure 5-bromophthalide in 37-40% yield.

IT 103146-25-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-bromophthalide via reduction of 4-bromophthalic anhydride)
RN 103146-25-4 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:546472 CAPLUS Full-text
DOCUMENT NUMBER: 141:106278
TITLE: A process for the preparation of racemic citalopram

diol and/or S- or R-citalopram diols and the use of such diols for the preparation of racemic citalopram R-citalopram and/or S-citalopram

INVENTOR(S): Petersen, Hans; Dancer, Robert; Christiansen, Brian; Humble, Rikke Eva

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004056754	A1	20040708	WO 2003-DK907		20031218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2511143	A1	20040708	CA 2003-2511143		20031218
AU 2003291960	A1	20040714	AU 2003-291960		20031218
EP 1581483	A1	20051005	EP 2003-767476		20031218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003017629	A	20051129	BR 2003-17629		20031218
CN 1729164	A	20060201	CN 2003-80107283		20031218
JP 2006511559	T	20060406	JP 2004-561086		20031218
ZA 2005004715	A	20060830	ZA 2005-4715		20050609
MX 2005PA06783	A	20050908	MX 2005-PA6783		20050621
IN 2005CN01364	A	20070622	IN 2005-CN1364		20050622
US 2006020140	A1	20060126	US 2005-540300		20050714
NO 2005003613	A	20050915	NO 2005-3613		20050725
PRIORITY APPLN. INFO.:			DK 2002-2004	A	20021223
			US 2002-436117P	P	20021223
			WO 2003-DK907	W	20031218

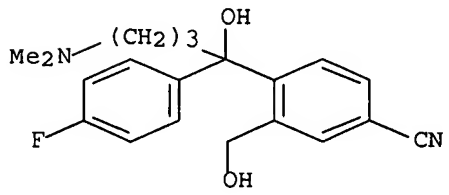
AB The invention relates to a process for the preparation of racemic citalopram diol [i.e., citalopram diol means 4-[4-(dimethylamino)-1-(4-fluorophenyl)- 1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile] and/or R- or S-citalopram diol, comprising the separation of a non-racemic mixture of R- and S-citalopram diol with more than 50% of one of the enantiomers into a fraction being enriched with S- or R-citalopram diol and a fraction comprising RS-citalopram diol wherein the ratio of R-citalopram diol:S-citalopram diol is equal to 1:1 or closer to 1:1 than in the initial mixture The method is characterized in that (i) RS-citalopram diol is precipitated from a solution of the initial non-racemic mixture, or R- or S-citalopram diol is dissolved into a solvent from the initial non-racemic mixture, leaving a residue of RS-citalopram diol, and in that (ii) the residue/precipitate formed is separated from the final solution phase, followed by optional steps of repetition, recrystn., purification, isolation and conversion between free base and salts. The invention also relates to a process for the preparation of RS-citalopram, S-citalopram or R-citalopram (all as free base and/or acid addition salt) comprising the method described above followed by ring closure.

IT 103146-25-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of racemic citalopram diol and/or S- or R-citalopram diols and the use of such diols for the preparation of racemic citalopram R-citalopram and/or S-citalopram)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:40088 CAPLUS Full-text

DOCUMENT NUMBER: 140:287145

TITLE: Enzymatic resolution of a quaternary stereogenic center as the key step in the synthesis of (S)-(+)-citalopram

AUTHOR(S): Solares, Laura F.; Brieva, Rosario; Quiros, Margarita; Llorente, Isidro; Bayod, Miguel; Gotor, Vicente

CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Facultad de Quimica, Universidad de Oviedo, Oviedo, 33071, Spain

SOURCE: Tetrahedron: Asymmetry (2004), 15(2), 341-345
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

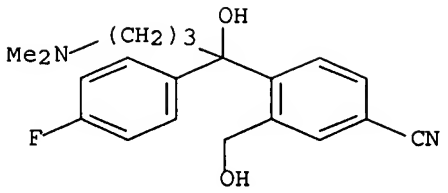
OTHER SOURCE(S): CASREACT 140:287145

AB The enzymic resolution of 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile, a useful intermediate in the synthesis of enantiomerically pure citalopram, has been studied. Candida antarctica lipase B (CAL-B) catalyzes the enzymic acetylation of the primary benzylic alc. with high enantioselectivity at the quaternary stereogenic center. This enzymic acetylation yielded the acetylated (+)-3-[(acetyloxy)methyl]-4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]benzonitrile and the desired (-)-4-[(1S)-4-(dimethylamino)-1- (4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. The enzymic enantioselective hydrolysis of the 3-acetyloxymethyl derivative catalyzed by CAL-B is also possible.

IT 103146-25-4, 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective, chemoselective enzymic acetylation and resoln. of [(dimethylamino)(fluorophenyl)(hydroxy)butyl](hydroxymethyl)benzonitrile as key step in synthesis of (S)-(+)-citalopram)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:58074 CAPLUS Full-text
DOCUMENT NUMBER: 138:122548
TITLE: Method for the preparation of escitalopram via chromatographic resolution of citalopram or its intermediates using carbohydrate-based chiral stationary phases
INVENTOR(S): Bech Sommer, Michael; Nielsen, Ole; Petersen, Hans; Ahmadian, Haleh; Pedersen, Henrik; Brosen, Peter; Geiser, Fiona; Lee, James; Cox, Geoffey; Dapremont, Olivier; Suteu, Christina; Assenza, Sebastian P.; Hariharan, Shankar; Nair, Usha
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006449	A1	20030123	WO 2002-DK491	20020712
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
TW 268926	B	20061221	TW 2002-91115430	20020711
CA 2451124	A1	20030123	CA 2002-2451124	20020712
AU 2002354525	A1	20030129	AU 2002-354525	20020712
EP 1409472	A1	20040421	EP 2002-750836	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002010817	A	20040622	BR 2002-10817	20020712
CN 1527825	A	20040908	CN 2002-813998	20020712
HU 200401451	A2	20041129	HU 2004-1451	20020712
HU 200401451	A3	20070529		
JP 2004538276	T	20041224	JP 2003-512221	20020712
ZA 2003009471	A	20041206	ZA 2003-9471	20031205

MX 2004PA00205	A	20040318	MX 2004-PA205		20040108
BG 108572	A	20050331	BG 2004-108572		20040209
IN 2004CN00293	A	20051209	IN 2004-CN293		20040212
US 2005065207	A1	20050324	US 2004-483824		20040930
PRIORITY APPLN. INFO.:			DK 2001-1101	A	20010713
			DK 2001-1851	A	20011211
			DK 2001-1852	A	20011211
			WO 2002-DK491	W	20020712

OTHER SOURCE(S): CASREACT 138:122548
GI

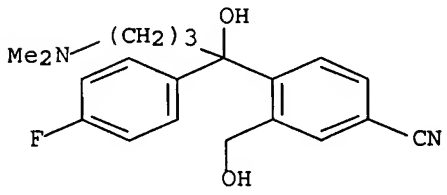
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A novel method is provided for the manufacture of the antidepressant escitalopram, i.e., (S)-I. The method comprises chromatog. separation of the enantiomers of either (1) citalopram, i.e., (±)-I, or (2) an intermediate in its production, using a chiral stationary phase such as Chiralpak AD or Chiralcel OD. Novel chiral intermediates for the synthesis of escitalopram, made by said method, are also provided. For example, the intermediate nitrile diol (±)-II was resolved using Chiralpak AD stationary phase on a Novasep Licosep 10-50 simulated moving bed chromatograph with MeCN mobile phase at 30°, to give both enantiomers of II with purity exceeding 99% ee. Similarly resolved in 96-99% yield and >99% ee were bromide diol (±)-III and bromophthalane (±)-IV, using Chiralpak AD and Chiralcel OD, resp. Resolution of (±)-IV was performed on a 500-g scale using 98:2 isohexane/isopropanol (vol/vol), and also on a smaller scale using supercrit. CO2 with MeOH/Et2NH/CF3CO2H modifier. The obtained bromide (S)-(+)-IV underwent cyanation by Zn(CN)2 and Pd(PPh3)4 according to the method of WO 00/13648, giving escitalopram in 80% yield and 99.6% ee.

IT 103146-25-4, 4-[4-(Dimethylamino)-1-(4-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)benzonitrile
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(resolution of; preparation of escitalopram via chromatog. resolution of citalopram or intermediates using carbohydrate-based chiral stationary phases)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:478150 CAPLUS Full-text
DOCUMENT NUMBER: 113:78150

TITLE: Preparation and isolation of antidepressant drug citalopram enantiomers and their pharmaceutical compositions

INVENTOR(S): Boegesoe, Klaus Peter; Perregaard, Jens

PATENT ASSIGNEE(S): Lundbeck, H., og Co. A/S, Den.

SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

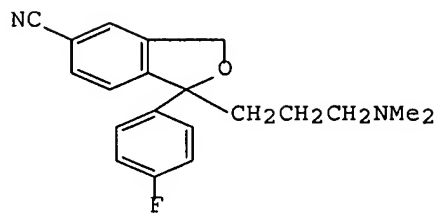
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 347066	A1	19891220	EP 1989-305532	19890601
EP 347066	B1	19950315		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8902599	A	19891215	DK 1989-2599	19890529
IL 90465	A	19950124	IL 1989-90465	19890530
AT 119896	T	19950415	AT 1989-305532	19890601
ES 2068891	T3	19950501	ES 1989-305532	19890601
FI 8902823	A	19891215	FI 1989-2823	19890608
FI 91527	B	19940331		
FI 91527	C	19940711		
US 4943590	A	19900724	US 1989-363589	19890608
NO 8902447	A	19891215	NO 1989-2447	19890613
NO 172892	B	19930614		
NO 172892	C	19930922		
AU 8936295	A	19900104	AU 1989-36295	19890613
AU 623144	B2	19920507		
ZA 8904476	A	19900425	ZA 1989-4476	19890613
CA 1339452	C	19970909	CA 1989-602683	19890613
JP 02036177	A	19900206	JP 1989-149752	19890614
JP 3044253	B2	20000522		
DK 9300115	A	19930201	DK 1993-115	19930201
DK 170280	B1	19950724		
US 34712	E	19940830	US 1993-122009	19930914
FI 9401829	A	19940420	FI 1994-1829	19940420
FI 113762	B1	20040615		
CA 1339568	C	19971202	CA 1997-617069	19970122
JP 11292867	A	19991026	JP 1999-46008	19990224
JP 3038204	B2	20000508		
FI 2000000507	A	20000306	FI 2000-507	20000306
FI 2004001359	A	20041020	FI 2004-1359	20041020

PRIORITY APPLN. INFO.:	GB 1988-14057	A	19880614
	FI 1989-2823	A	19890608
	US 1989-363589	A5	19890608
	CA 1989-602683	A3	19890613
	JP 1989-149752	A3	19890614

OTHER SOURCE(S): MARPAT 113:78150

GI



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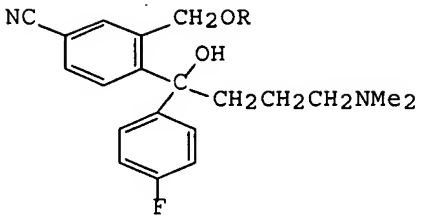


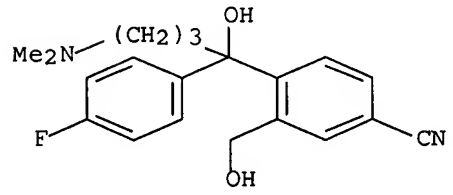
II

AB The title compound (I) in pure (+)-enantiomer form and its racemic mixture, useful as antidepressants, geriatrics, or in treatment of obesity and alcoholism, are prepared SOCl2 was refluxed with a solution of (+)-CF3CH(OMe)CO2H in CHCl3 to give the acid chloride, which was diluted with CH2Cl2 and treated with benzyl alc. derivative II (R = H) and Et3N to give ester II [R = CF3CH(OMe)CO] (III) as a diastereomeric mixture, which was purified by HPLC to give a pure enantiomer. III was dissolved in MePh and treated with Me3COK in MePh at 0° to give (+)-I of 99.6% optical purity, which showed ED50 of 2.0 μmol/kg for 5-HTP potentiation in mice and IC50 of 1.1 nM against 5-HT uptake, vs. 3.3 μmol/kg and 1.8 μM, resp., with (±)-I. Similarly prepared (-)-I showed much lower activity. Tablet, syrup, and injection formulations were given.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	125.40	125.61

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.82	-14.82

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:05:58 ON 25 SEP 2007